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本署檔號 OUR REF.: DH DO PRIE/7-30/15
(來函請註明此檔案號碼)
(IN REPLY PLEASE QUOTE THIS FILE REF.)

DEPARTMENT OF HEALTH
DRUG OFFICE
DRUG REGISTRATION AND
IMPORT/EXPORT CONTROL DIVISION
3/F., Public Health Laboratory Centre,
382 Nam Cheong Street, Kowloon, Hong Kong

BY FAX

28 January 2013

Dr. Donald LI
President
Hong Kong Academy of Medicine
(Fax Number: 2505 5577)

Dear Dr. LI,

US FDA : Potential risk of liver injury associated with the use of Samsca (tolvaptan)

Your attention is drawn to US Food and Drug Administration (FDA) announcement with respect to significant liver injury associated with the use of Samsca.

In a double-blind, 3-year, placebo-controlled trial in about 1400 patients with Autosomal Dominant Polycystic Kidney Disease (ADPKD) and its open-label extension trial, 3 patients treated with the drug developed significant increases in serum alanine aminotransferase (ALT) with concomitant, clinically significant increases in serum total bilirubin. In the trials the maximum daily dose of Samsca administered (90 mg in the morning and 30 mg in the afternoon) was higher than the maximum 60 mg daily dose approved for the treatment of hyponatremia.

Most of the liver enzyme abnormalities were observed during the first 18 months of therapy. Following discontinuation of treatment, all 3 patients improved. An external panel of liver experts assessed these 3 cases as being either probably or highly likely to be caused by tolvaptan. These findings indicate that Samsca (tolvaptan) has the potential to cause irreversible and potentially fatal liver injury. These data are not adequate to exclude the possibility that patients receiving Samsca for its indicated use of clinically significant hypervolemic and euvolemic hyponatremia are at a potential increased risk for irreversible and potentially fatal liver injury.

Samsca is a selective vasopressin V2-receptor antagonist indicated for the treatment of clinically significant hypervolemic and euvolemic hyponatremia. Samsca is not approved for the treatment of ADPKD.

Healthcare providers should perform liver tests promptly in patients who report symptoms that may indicate liver injury, including fatigue, anorexia, right upper abdominal discomfort, dark urine or jaundice. If hepatic injury is suspected, Samsca should be promptly discontinued, appropriate treatment should be instituted, and investigations should be performed to determine probable cause. Samsca should not be re-initiated in patients unless the cause for the observed liver injury is definitively established to be unrelated to treatment with Samsca.

Please refer to the following website in FDA for details: http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm336669.htm

In Hong Kong, Samsca Tablet 15mg (HK-59910) and 30mg (HK-59911) are registered by Otsuka Pharmaceutical Co Ltd. They are prescription-only medicines and are indicated for the treatment of clinically significant hypervolemic and euvolemic hyponatremia.

Please encourage your members to report any adverse events caused by the drugs to the Pharmacovigilance Unit of Department of Health (tel. no.: 2319 2920, fax: 2186 9845 or email: adr@dh.gov.hk). For details, please refer to the website at Drug Office under "ADR Reporting": http://www.drugoffice.gov.hk/adr.html. You may wish to visit the Drug Office's website for subscription and browsing of "Drug News" which is a monthly drug safety digest of drug safety news and information issued by Drug Office.

Yours sincerely,

(H F LEE)
for Assistant Director (Drug)